

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP2004/005456

## A. CLASSIFICATION OF SUBJECT MATTER

Int.Cl<sup>7</sup> A61K45/00, 38/00, 31/517, A61P27/02

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Int.Cl<sup>7</sup> A61K45/00, 38/00, 31/517, A61P27/02

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

MEDLINE CAPLUS EMBASE BIOSIS (STN) JMEDPLUS (JOIS)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	NEGISHI M. et al., 'Regulation of neurite formation by Rho family GTPases.', Seikagaku. Journal of Japanese Biochemical Society, 2002 May; 74(5): 395-8. [Japanese]	1-12
X	Nikolic M. 'The role of Rho GTPases and associated kinases in regulating neurite outgrowth.' Int J. Biochem Cell Biol. 2002 July; 34(7): 731-45.	1-12
X	Lehmann M. et al., 'Inactivation of Rho signaling pathway promotes CNS axon regeneration.' J Neurosci. 01 September, 1999 (01.09.99); 19(17): 7537-47.	1-12

 Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier application or patent but published on or after the international filing date	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&" document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search  
07 June, 2004 (07.06.04)Date of mailing of the international search report  
22 June, 2004 (22.06.04)Name and mailing address of the ISA/  
Japanese Patent Office

Authorized officer

Facsimile No.

o.

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## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Dergham P. et al., 'Pho signaling pathway targeted to promote spinal cord repair.' J Neurosci. 01 August, 2002 (01.08.02): 22(15): 6570-7.	1-12
X	US 2002/0119140 A1 (Lisa McKerracher), 29 August, 2002 (29.08.02), Full text (Family: none)	1-12
X	WO 02/083175 A1 (Senju Pharmaceutical Co., Ltd.), 24 October, 2002 (24.10.02), Full text & EP 1378247 A1	1-12
X	WO 01/068607 A1 (Mitsubishi Pharma Corp.), 20 September, 2001 (20.09.01), Full text & EP 1270570 A1	1-12
X	JP 2003-073357 A (Mitsubishi Pharma Corp.), 12 March, 2003 (12.03.03), Full text (Family: none)	1-12
Y	WO 02/076977 A2 (BAYER CORP.), 23 October, 2002 (23.10.02), Example 1 (Family: none)	1-12
Y	WO 02/100833 A1 (Sumitomo Pharmaceuticals Co., Ltd.), 19 December 2002 (19.12.02), Example 1 (Family: none)	1-12
Y	JP 2000-044513 A (Santen Pharmaceutical Co., Ltd.), 15 February, 2000 (15.02.00), Par. No. [0024]; compound 3 & EP 1094055 A1	1-12

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**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: 13-16

because they relate to subject matter not required to be searched by this Authority, namely:

Claims 13 to 16 pertain to methods for treatment of the human body by therapy and thus relate to a subject matter which this International Searching Authority is not required, under the provisions of Article 17(2) (a) (i) of the PCT and Rule 39.1(iv) of the Regulations under the PCT, to search.

2.  Claims Nos.:

because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3.  Claims Nos.:

because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

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**<Subject of search>**

Claims 1 to 12 relate to a corneal neurite formation promoter, a corneal nerveaxon extension promoter, a corneal perception repairing agent and a remedy for dry eye each containing, as the active ingredient, a compound defined by a desired property as "an Rho protein inhibitor". Thus, claims 1 to 12 involve any compounds having this property in the scopes thereof. However, it is recognized that only small part of the claimed compounds are exclusively disclosed in the description in the meaning within PCT Article 5 and thus these claims are not supported by the disclosure in the description in the meaning within PCT Article 6.

Even though the common technical knowledge at the point of the application is taken into consideration, it cannot be recognized that the scope of compounds having the above property as "an Rho protein inhibitor" could be specified. Thus, claims 1 to 12 do not comply with the requirement of clearness as defined in PCT Article 6 too.

Therefore, the search was made on relationships among the inhibition of Rho protein and promotion of corneal neurite formation, promotion of corneal nerveaxon extension, repair of corneal perception and treatment for dry eye, as well as corneal neurite formation promoters, corneal nerveaxon extension promoters, corneal perception repairing agents and remedies for dry eye containing, as the active ingredient, the C3 enzyme and ROCK inhibitors of compounds 1 to 4 which are specifically illustrated in the description.